



527 Rec'd PCT/P 07 DEC 2000

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A33477 PCT USA - 062635.0125

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : So et al.
Serial No. : 09/673,872
Filed : October 23, 2000
For : PHARMACEUTICAL COMPOSITION

CLAIM FOR PRIORITY UNDER 35 U.S.C. § 119

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

A claim for priority is hereby made under the provisions of 35 U.S.C. § 119 for the above-identified PCT application based upon Australian application PP 3107 filed April 22, 1998, and International Application PCT/AU99/00294 filed April 20, 1999.

Respectfully submitted,

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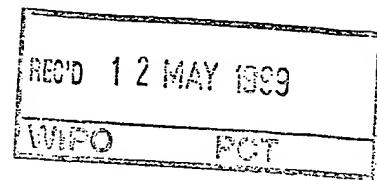
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I, KIM MARSHALL, MANAGER EXAMINATION SUPPORT AND SALES,
hereby certify that the annexed is a true copy of the Provisional specification in
connection with Application No. PP 3107 for a patent by SOLTEC RESEARCH
PTY LTD filed on 22 April 1998.

PRIORITY DOCUMENT

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WITNESS my hand this Fourth
day of May 1999

KIM MARSHALL
MANAGER EXAMINATION SUPPORT AND
SALES

Vehicle System for a Composition Comprising a Piperidinopyrimidin Derivative

Background of the invention

5 The present invention relates to a novel vehicle system for a composition comprising a Piperidinopyrimidine derivative or a pharmaceutically acceptable salt. More particularly, the present invention relates to a novel vehicle system for a composition comprising a Piperidinopyrimidine derivative where the Piperidinopyrimidine derivative is minoxidil. Minoxidil is a well known pharmaceutical active ingredient having several indications
10 including use as a hair growth stimulant.

Minoxidil has poor solubility in water and ethanol and pharmaceutical preparations currently marketed only contain a small percentage of minoxidil. That is, below 5%.

15 Numerous formulations comprising minoxidil have been published including United States patents 4820512, 5104646, 5225189, 4938953, 4596812, 5006332, 5156836 and 5643942. Many of the formulations require (or would require where the amount of minoxidil is greater than 5%) a very high percentage (often in the range of 30-50%) of propylene glycol or a similar glycol product in order to improve the solubility of minoxidil.
20 Due to the viscosity and stickiness of propylene glycol, large amounts of propylene glycol or similar agents in a composition are not pharmaceutically or cosmetically elegant and may be unacceptable to the consumer. In addition, high concentrations of propylene glycol may cause local irritation and hypersensitivity upon application to the scalp.

25 Surprisingly, the inventors have discovered that by adjusting the pH and the ratio of water and lower alcohol in the solvent, a vehicle system exists which can dissolve amounts of

minoxidil up to 5% and greater without the need of large amounts of propylene glycol or similar agents.

Summary of the invention

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Accordingly, there is provided in the invention a vehicle system for a composition comprising a Piperidinopyrimidine derivative or a pharmaceutically acceptable salt where said system comprises 0-15% of propylene glycol, up to 20% of a non-ionic surfactant and a solvent which comprises a mixture of water and a lower alcohol, where said
10 composition has a pH of 7.0 or less.

Detailed description of the invention

Preferably the Piperidinopyrimidine derivative is minoxidil. The amount of minoxidil can
15 be ranged from 0.1% to 20%. Preferably the amount of minoxidil is greater than 5%.

Preferably the lower alcohol is ethanol. The ratio of water to ethanol is preferably from 1:1 to 1:3, more preferably 1:1.7 to 1:1.9.

20 The non-ionic surfactant is preferably in amounts of less than 5%, more preferably less than 2.0%. The preferred non-ionic surfactant is a C12-C15 fatty alcohol with approximately 4 moles of ethylene oxide per mole of alcohol and contains up to 23 moles of ethylene oxide and is biodegradable to a level greater than 90%.

25 The pH of the composition is preferably between 5-7, more preferably between 6.0-6.5. Any suitable acid may be used to adjust the pH, including mineral acids such as

hydrochloric acid, sulphuric acid, nitric acid and phosphoric acid or organic acids such as citric acid, acetic acid or maleic acid.

In compositions comprising 5% of minoxidil or greater, it is preferred to include benzyl alcohol in the composition. The benzyl alcohol may be in amounts of up to 50%.

The final presentation of the composition may be any suitable preparation and may include solutions, lotions, ointments, mousses, foams, sprays, aerosols, shampoos and/or conditioners, gels and other preparations known in the art.

10

Examples of suitable compositions in accordance with the invention but not limited to the invention include:

Example 1

15 Topical Minoxidil lotion 5% with no propylene glycol

Minoxidil	5.00%
Ethanol	60.3%
Polysorbate 60	0.4%
Polyoxyethylene lauryl alcohol	1.00%
20 Acetic Acid	qs. pH 6.0
Purified Water	to total 100%

Example 2

Topical Minoxidil mousse 5% for hair treatment

25	Minoxidil	5.00%
	Cetyl Alcohol	2.20%
	Stearyl Alcohol	1.00%
	Ethanol	51.8%
	Polysorbate 60	0.4%
30	Polyoxyethylene lauryl alcohol	1.00%
	Propylene Glycol	5.00%

Propellant P75	4.30%
Acetic Acid	qs. pH 6.0
Purified water	to total 100%

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Example 3Topical Minoxidil lotion 8% for hair treatment

10	Minoxidil	8.00%
	Ethanol	50.50%
	Polysorbate 60	0.4%
	Polyoxyethylene lauryl alcohol	1.00%
	Nitric Acid	qs. pH 6.0
15	Propylene Glycol	7.30%
	Benzyl Alcohol	5.00%
	Purified water	to total 100%

Example 4

20	<u>Topical Minoxidil lotion 10% for hair treatment</u>	
	Minoxidil	10.00%
	Ethanol	48.0%
	Polysorbate 60	0.4%
	Polyoxyethylene lauryl alcohol	1.00%
25	Acetic Acid	qs. pH 6.0
	Propylene Glycol	10.0%
	Benzyl Alcohol	5.00%
	Purified water	to total 100%

30 Example 5Topical Minoxidil lotion 10% for hair treatment

	Minoxidil	10.00%
	Ethanol	47.50%
	Polysorbate 60	0.4%
35	Polyoxyethylene lauryl alcohol	1.00%
	Acetic Acid	qs. pH 6.0

Benzyl Alcohol	15.00%
Purified water	to total 100%

Example 6

5 Topical Minoxidil lotion 11% for hair treatment

Minoxidil	11.00%
Ethanol	44.20%
Polysorbate 60	0.4%
Polyoxyethylene lauryl alcohol	1.00%
10 Acetic Acid	qs. pH 6.0
Benzyl Alcohol	20.00%
Purified water	to total 100%

Example 7

15 Topical Minoxidil lotion 12% for hair treatment.

Minoxidil	12.00%
Ethanol	42.7%
Polysorbate 60	0.4%
Polyoxyethylene lauryl alcohol	1.00%
20 Acetic Acid	qs. pH 6.0
Benzyl Alcohol	20.00%
Purified water	to total 100%

Example 8

25 Topical Minoxidil lotion 12% for hair treatment

Minoxidil	12.00%
Ethanol	42.7%
Polysorbate 60	0.4%
Polyoxyethylene lauryl alcohol	1.00%
30 Acetic Acid	qs. pH 6.0
Benzyl Alcohol	10.00%
Propylene Glycol	10.00%
Purified water	to total 100%

35 Example 9

Topical Minoxidil lotion 12% for hair treatment

	Minoxidil	12.00%
	Ethanol	42.7%
	Polysorbate 60	0.4%
	Polyoxyethylene lauryl alcohol	1.00%
5	Acetic Acid	qs. pH 6.0
	Benzyl Alcohol	15.00%
	Propylene Glycol	5.00%
	Purified water	to total 100%

10

All the above examples were stored at room temperature and no crystallisation or precipitation was observed for at least 10 days.

Please note that all percentages are based upon the total weight of the composition
15 unless otherwise specified.

20 SOLTEC RESEARCH PTY LTD

Date: 22 APRIL 1978